Original Investigation

# Risk of Critical Illness Among Patients With Solid Cancers
## A Population-Based Observational Study

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**IMPORTANCE** Critical illness may be a potential determinant of cancer outcomes and geographic variations, but its role has not been described before.

**OBJECTIVE** To determine the incidence of admission to intensive care units (ICUs) within 2 years following cancer diagnosis.

**DESIGN, SETTING, AND PARTICIPANTS** This was a retrospective observational study using cancer registry data in 4 datasets from 2000 to 2009 with linked ICU admission data from 2000 to 2011, in the West of Scotland region of the United Kingdom (population, 2.4 million; all 16 ICUs within the region). All 118 541 patients (≥16 years) diagnosed as having solid (nonhematological) cancers. Their median age was 69 years, and 52.0% were women.

**MAIN OUTCOMES AND MEASURES** Demographic and clinical variables associated with admission to an ICU and death in an ICU.

**RESULTS** A total of 118 541 patients met the study criteria. Overall, 6116 patients (5.2% [95% CI, 5.0%-5.3%]) developed a critical illness and were admitted to an ICU within 2 years. Risk of critical illness was highest at ages 60 to 69 years and higher in men. The cumulative incidence of critical illness was greatest for small intestinal (17.2% [95% CI, 13.3%-21.8%]) and colorectal cancers (16.5% [95% CI, 15.9%-17.1%]). The risk following breast cancer was low (0.8% [95% CI, 0.7%-1.0%]). The percentage who died in ICUs was 14.1% (95% CI, 13.3%-15.0%), and during the hospital stay, 24.6% (95% CI, 23.5%-25.7%). Mortality was greatest among emergency medical admissions and lowest among elective surgical patients. The risk of critical illness did not vary by socioeconomic circumstances, but mortality was higher among patients from deprived areas.

**CONCLUSIONS AND RELEVANCE** In this study, about 1 in 20 patients experienced a critical illness resulting in ICU admission within 2 years of cancer diagnosis. The associated high mortality rate may make a significant contribution to overall cancer outcomes.

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Survival from most cancers has improved, but international variations persist, with poorer survival in the United Kingdom than other developed countries. Variations in outcomes manifest soon after diagnosis. For example, socioeconomic variations in survival from colorectal cancers are largely confined to excess mortality in the postoperative period, and international variations in breast cancer survival are most pronounced in the first month and year after diagnosis.[1,2] However, it remains unclear what mediates better survival. It has been suggested that quality of health care may explain international variations in cancer outcomes.[3] While this is often considered in terms of availability and effectiveness of therapeutic interventions, the role of supportive care to prevent or ameliorate critical illness among patients with cancer may also be important.

The development of a critical illness requiring support in an intensive care unit (ICU) has received relatively little attention for patients with cancer. ICUs provide enhanced physiological monitoring and support of organ system failure, with higher than normal staff-to-patient ratios and greater costs.[4] ICU care is physically and psychologically traumatic and is associated with persisting morbidity after discharge.[5,6] The United Kingdom has considerably lower provision of ICU beds, at 3.5 per 100 000 population, than other European countries, North America, and Australasia.[7] Among the EUROCARE countries, those with consistently better survival, such as France and Belgium, have 3 to 6 times the number of ICU beds per head of population than the United Kingdom.[3,7]

About 1 in 7 ICU patients has a malignant neoplasm, but it is not known, at present, whether the persisting effects of critical illness and ICU care interfere with planned cancer treatment or contribute to overall survival.[8] A recent systematic review[9] reported an average ICU mortality of 31% and hospital mortality of 38%, although outcomes varied by cancer site, type of admission (whether planned or emergency) and specialty. Development of a critical illness requiring ICU support may be an important clinical event that contributes to poorer overall survival. It would therefore be useful to understand which patients with cancer are at greatest risk of critical illness as a basis for identifying how this might be prevented or detected earlier. To our knowledge, however, research has not been published that evaluates the risks of critical illness requiring ICU admission among patients with cancer.

The aim of our study was to describe risks of critical illness resulting in ICU admission among patients with solid cancers. We performed a population-based study using linked cancer registry, hospitalization, ICU audit, and death records to determine risks after a cancer diagnosis.

**At a Glance**

- More than 6000 patients out of more than 118 500 with cancer (5%) had been admitted to an ICU within 2 years of incident cancer between 2000 and 2009.
- The risk of admission was highest among patients with gastrointestinal cancer and lowest in those with prostate cancer, breast cancer, and melanoma of skin.
- Mortality after admission was highest among emergency medical admissions and lowest among elective surgical admissions.
- Hospital mortality was often high among those with cancers with otherwise good prognoses, such as breast and colorectal cancer.
- Critical illness may make an important contribution to overall cancer outcomes.

## Methods

### Data Source

In this retrospective observational study we identified patients resident in the West of Scotland region who had a diagnosis of a malignant cancer on the Scottish Cancer Registry between 2000 and 2009, and we investigated whether they had been admitted to 1 of the 16 general ICUs located in the region within 2 years after the date of cancer incidence.

We used linked data from 4 Scottish data sets: the Scottish Cancer Registry, Scottish Morbidity Record 01 (SMR01), National Records of Scotland death records, and WardWatcher ICU database. The Scottish Cancer Registry collects information on all new cases of cancer, including primary malignant neoplasms, carcinoma in situ, neoplasms of uncertain behavior, and benign brain and spinal cord tumors. Cancer diagnoses are coded to the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10)*. The registry is linked by the Information Services Division (ISD) of NHS National Services Scotland using probabilistic linkage procedures to inpatient and day case discharge summaries from nonobstetric, nonpsychiatric specialties in general acute NHS hospitals (SMR01), National Records of Scotland death records, and to the Scottish Intensive Care Society Audit Group (SICSAG) WardWatcher ICU audit database.

The SICSAG WardWatcher audit system is used in ICUs throughout Scotland and collects data on patient demographic details, admitting specialty, admission diagnosis, the patient's prior location, comorbidities, and type of organ support. The SICSAG episodes were matched to SMR01 stays using the dates of hospital and ICU admission and discharge. This allowed identification of type of hospital admission, admitting specialty, and discharge type.

### Setting

The West of Scotland region of the United Kingdom has a population of 2.4 million. It is predominantly urban, with most of the population living in large towns or the city of Glasgow. There were 16 general ICUs in the area during the study period. Some functioned as a combined ICU/high-dependency unit (HDU) for some or all of the period.

In the United Kingdom, ICU level care is provided to patients with multiorgan failure or single-organ respiratory failure needing advanced respiratory support . The nursing staff to patient ratio is 1:1, and HDU care is available to patients with single-organ failure or those requiring high-intensity observation. The nurse to patient ratio is approximately 1:2. Beyond professional guidelines, there are no absolute criteria for admission to a critical care area. The final decision rests with the admitting clinician. Generally, patients who have a terminal illness, refuse admission, or have a do not resuscitate order would not be admitted.

### Study Population

We included patients if they were 16 years or older, resided in the West of Scotland, and had a diagnosis of a solid tumor (*ICD-10* codes C00-C80, ignoring nonmelanoma skin cancer code C44) in the Scottish Cancer Registry from January 1, 2000, through December 31, 2009. We identified if patients were admitted to a general ICU up to 2 years after the date of incidence. If a patient had more than 1 ICU admission, we used the first ICU admission. For simplicity, patients who had more than 1 cancer were grouped separately. The incidence date of the earliest diagnosed tumor was used in cases of multiple cancers. We excluded patients who had brain, other central nervous system, and intracranial tumors (*ICD-10* codes C71-C72, D32-D33, D35.2-D35.4, D42-D43, D44.3-D44.5) because they are more likely to be admitted to a specialized ICU. Patients with hematological cancers (*ICD-10* codes C81-C96, D45-D47) were excluded because there was a series of important changes in guidance for treatment and support of patients with hematological malignant neoplasms over the study period.[10]

This study was approved by the West of Scotland Research and Ethics Committee. Approvals to use the data were obtained from the West of Scotland Critical Care Research Network, SICSAG, and the West of Scotland Cancer Surveillance Unit.

Table 1. Incident Cancers by Age Group, Showing Percentage Admitted to ICU Within 2 Years of Diagnosis, Percentage Who Received Organ Support, and Hospital Admission Specialty, 2000 to 2009[a]

| | | Patients Admitted to ICU | | Hospital Admission Specialty of Patients Who Received Organ Support[b] | |
|---|---|---|---|---|---|
| Total Patients With Cancer, Age Group, y (No. of Patients) | Patients Admitted to ICU | Emergency Hospital Admission | Received Organ Support | Medical | Surgical |
| 16-29 (1163) | 26 (2.2) | 10 (38.5) | 17 (65.4) | 4 (23.5) | 13 (76.5) |
| 30-39 (3128) | 90 (2.9) | 45 (50.0) | 48 (53.3) | 12 (25.0) | 36 (75.0) |
| 40-49 (7844) | 371 (4.7) | 158 (42.6) | 206 (55.5) | 48 (23.3) | 156 (75.7) |
| 50-59 (17 690) | 985 (5.6) | 384 (39.0) | 618 (62.7) | 117 (18.9) | 494 (79.9) |
| 60-69 (30 749) | 1945 (6.3) | 781 (40.2) | 1151 (59.2) | 216 (18.8) | 921 (80.0) |
| 70-79 (35 423) | 1938 (5.5) | 829 (42.8) | 1159 (59.8) | 210 (18.1) | 936 (80.8) |
| 80-89 (19 557) | 712 (3.6) | 382 (53.7) | 397 (55.8) | 71 (17.9) | 322 (81.1) |
| >90 (2987) | 49 (1.6) | 40 (81.6) | 28 (57.1) | 7 (25.0) | 21 (75.0) |
| All (118 541) | 6116 (5.2) | 2629 (43.0) | 3624 (59.3) | 685 (18.9) | 2899 (80.0) |

Abbreviation: ICU, intensive care unit.

[a] Data are given as number (percentage).

[b] Percentages do not sum to 100% because some ICU patients could not be matched to a hospital admission record.

## Statistical Analysis

Age- and sex-specific cumulative counts of numbers of ICU admissions expressed as a percentage of the incident cancer population were calculated by time since diagnosis. We compared the percentage of patients admitted to ICU by cancer type. We investigated ICU admission by hospital admission type dichotomized as emergency or elective, specialty at hospital admission dichotomized as medical or surgical, and by receipt of organ support. Organ support was defined as invasive mechanical ventilation via endotracheal tube or tracheostomy, use of inotropic or vasopressor medication, or renal replacement therapy of any modality. The Scottish Index of Multiple Deprivation (SIMD) was used as an area-level measure of socioeconomic status. The SIMD is the Scottish Government's official tool for identifying deprived places in Scotland.[11] The SIMD uses 7 domains (employment, income, heath, education, access to services, crime, and housing) to rank 6505 small geographical areas of Scotland from 1 (most deprived) to 6505 (least deprived). These were grouped into national quintiles labeled 1 (most deprived) to 5 (least deprived).

Organ support data prior to 2005 were not complete. We visited ICU sites to obtain these data, but a high proportion of missing data remained. Receipt of any organ support could not be fully ascertained for 15% of patients prior to 2005 mainly because of incomplete renal support data. The number who received organ support prior to 2005 was therefore underestimated; however, the proportion of patients who received renal support only was small (0.8% of patients admitted after 2004), and thus we do not feel that the missing organ support data would substantially bias our findings.

Five centers were combined ICU/HDU units, and we could not differentiate patients admitted to ICU from those admitted to an HDU. We used receipt of organ support to differentiate patients. The APACHE II severity of disease score was recorded for 70% of patients admitted to an ICU.[12] WardWatcher recorded deaths that occurred in an ICU. Patients who died during the hospital stay in which the ICU admission occurred were identified from the SMR01 discharge summary or WardWatcher database. A total of 76 ICU stays (1.2%) among patients with cancer could not be matched to an SMR01 stay. We limited the analysis of mortality to the 6040 patients with matched ICU and SMR01 records.

Statistical analyses were performed using Stata software (version 13; StataCorp LP). Unless otherwise stated, we described medians with interquartile ranges (IQR) and percentages with exact 95% CIs and used a conventional level of .05 to indicate statistical significance. We used fixed- and mixed-effects logistic regression to analyze trends in mortality with calendar year and to investigate variation between ICU units.

# Results

Between 2000 and 2009, 118 541 patients were diagnosed as having a cancer and were eligible for inclusion in study. The median age was 69 years (IQR, 59-77 years), and 61 607 (52.0%) were women. Those 60 years or older accounted for three-quarters of patients (74.8%) (**Table 1**).

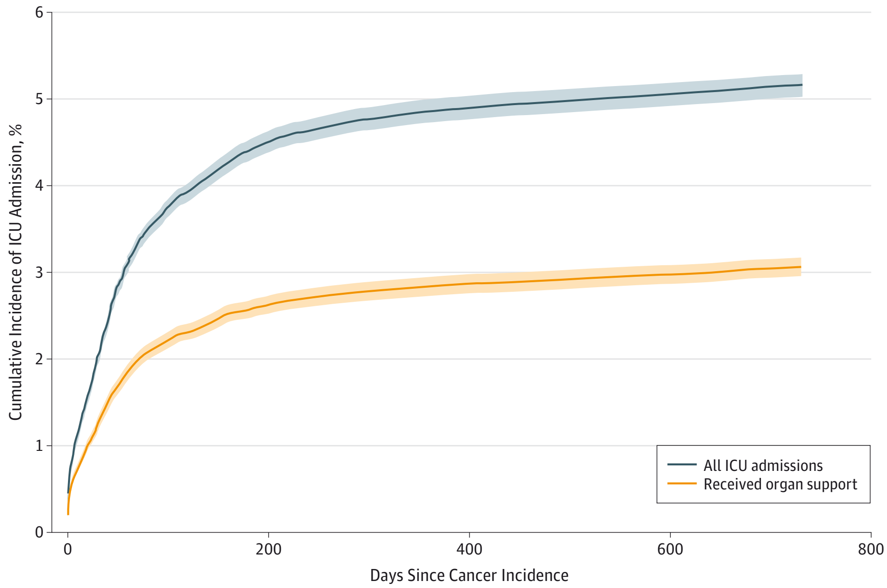
## Admission to ICU

Within 2 years of diagnosis, 6116 patients (5.2% [95% CI, 5.0%-5.3%]) experienced a critical illness resulting in admission to ICU. Their median age was 68 years (IQR, 60-75 years), and 2542 (41.6%) were women. The APACHE II score was recorded for 4279 patients (70.0%) (median score, 17; IQR, 13-22). Following cancer diagnosis, the cumulative incidence of ICU admission (**Figure**) increased sharply to 3.7% (95% CI, 3.6%-3.9%) by 100 days. By 200 days the cumulative incidence continued to increase, but more slowly, to 4.5% (95% CI, 4.4%-4.6%).

Admission to an ICU occurred during an emergency hospital stay for 43.0% of patients. Organ support was received by 59.3% of admitted patients, or 3.1% (95% CI, 3.0%-3.2%) of all patients with cancer. Among patients who received organ support, 18.9% had been admitted to a medical specialty at hospital admission. The proportion admitted to a medical specialty was higher at younger ages than at older ages.

Admission to an ICU increased with increasing age, rising from 2.2% (95% CI, 1.5%-3.3%) at ages 16 to 29 years to a maximum of 6.3% (95% CI, 6.1%-6.6%) at ages 60 to 69 years and

Figure. Cumulative Incidence of Admission to Intensive Care Units (ICUs) by Time Since Cancer Incidence Date




Shaded areas indicate 95% CIs.

declined thereafter. The risk of critical illness was higher in men than in women for all age groups (see eFigure 1 in the Supplement). The age-specific pattern of admissions in which patients received organ support was similar to the overall pattern of ICU admission, but proportions were lower at all ages.

There was a decline in proportions of patients with cancer diagnosed from 2000 to 2009 who developed a critical illness and were admitted to an ICU within 2 years (eFigure 2 in the Supplement). The decline was greater among patients who did not receive organ support; there were smaller reductions in ICU admissions for patients who required organ support.

The cumulative incidence of critical illness and ICU admission following diagnosis of specific solid cancers are shown in **Table 2**. The most frequent cancers were lung, breast, and colorectal malignant neoplasms. The risks were greatest for small intestinal and colorectal cancers (17.2% [95% CI, 13.3%-21.8%] and 16.5% [95% CI, 15.9%-17.1%], respectively) followed by stomach (11.3% [95% CI, 10.3%-12.3%]) and head and neck cancers (12.8% [95% CI, 11.9%-13.8%]). Cancer stage was not recorded for most cancer sites but was available for 77.7% of colorectal cancers (12 071 of 15 535). Admission to an ICU was higher among patients with Dukes stage B and C colorectal cancer (22.9% [95% CI, 21.6%-24.3%] and 23.8% [95% CI, 22.4%-25.3%, respectively) compared with Dukes stage A or D (15.8% [95% CI, 14.1%-17.6%] and 9.6% [95% CI, 8.6%-10.7%]). Two-fifths (41.9%) of all ICU admissions among patients with solid cancers occurred in those with colorectal cancers, with those with head and neck and stomach cancers contributing 10.4% and 7.4%, respectively. Although breast cancer had a high incidence, the risk of critical illness was among the lowest for all malignant neoplasms, at 0.8% (95% CI, 0.7%-1.0%).

The proportion of admissions to ICUs that occurred during an emergency hospital admission varied from a low of 25.3% for kidney and head and neck cancers, to 78.2% and 85.1% of patients with cancers of the small intestine and unknown primary, respectively.

Receipt of organ support varied by cancer type, from a low of 47.8% (95% CI, 45.9%-49.8%) of patients with colorectal cancer to 91.5% (95% CI, 89.1%-93.6%) of those with head and neck cancer. Most patients with cancer (80.0%) who received organ support were surgical patients, but there was substantial variation by cancer type. Over 85% of those with colorectal, head and neck, stomach, bladder, kidney, and esophageal cancer were admitted from surgical specialties. In contrast, over 40% of those with breast, lung, melanoma, ovary, cervical, and cancers of unknown origin were medical admissions.

Seventy percent of ICU patients were admitted within 3 months of the date of cancer incidence (eTable 1 in the Supplement). Notable exceptions include breast, bladder, prostate, and testicular cancer when around 37% or less were admitted within 3 months. Cancers with poorer survival, such as lung, liver, and ovarian malignant neoplasms, had the highest proportions of ICU admissions within 3 months of incidence, at 75.6%, 77.6%, and 87.7%, respectively. Patients who were medical admissions were more likely to be admitted to ICU within 14 days of cancer incidence compared with patients admitted to surgical specialties (38.6% compared with 23.2%; $P < .001$).

## Mortality

A total of 852 of 6040 patients with cancer (14.1% [95% CI, 13.2%-15.0%]) died during their stay in an ICU. Mortality varied by type of hospital admission, specialty, and organ support (**Table 3**). Mortality among patients who received organ support was approximately 10 times that experienced by patients who did not (22.2% [95% CI, 20.9%-23.6%] compared with 2.3% [95% CI, 1.8%-3.0%]). The proportion of deaths among the 685 medical patients who received organ support

Table 2. ICU Admissions Within 2 Years of Cancer Incidence by Cancer Type, 2000 to 2009[a]

| Type of Cancer (No. of Patients) | All Patients With Cancer Admitted to ICU | Patients Admitted to ICU: Emergency Hospital Admission | Patients Admitted to ICU: Received Organ Support | Hospital's Admission Specialty of Patients Who Received Organ Support[b]: Medical | Hospital's Admission Specialty of Patients Who Received Organ Support[b]: Surgical |
|---|---|---|---|---|---|
| Colorectal (15 535) | 2561 (16.5) | 1167 (45.6) | 1225 (47.8) | 134 (10.9) | 1074 (87.7) |
| Head and neck (4958) | 636 (12.8) | 164 (25.8) | 582 (91.5) | 47 (8.1) | 533 (91.6) |
| Stomach (4045) | 456 (11.3) | 129 (28.3) | 234 (51.3) | 34 (14.5) | 199 (85.0) |
| Esophagus (3815) | 389 (10.2) | 74 (19.0) | 255 (65.6) | 21 (8.2) | 231 (90.6) |
| Lung (23 443) | 381 (1.6) | 230 (60.4) | 285 (74.8) | 138 (48.4) | 145 (50.9) |
| Kidney (3054) | 249 (8.2) | 63 (25.3) | 137 (55.0) | 14 (10.2) | 120 (87.6) |
| Bladder (3523) | 182 (5.2) | 68 (37.4) | 115 (63.2) | 13 (11.3) | 101 (87.8) |
| Breast (17 591) | 149 (0.8) | 94 (63.1) | 93 (62.4) | 37 (39.8) | 53 (57.0) |
| Ovary (2910) | 138 (4.7) | 84 (60.9) | 68 (49.3) | 42 (61.8) | 26 (38.2) |
| Prostate (11 337) | 136 (1.2) | 71 (52.2) | 85 (62.5) | 25 (29.4) | 58 (68.2) |
| Cervix and corpus uteri (3721) | 113 (3.0) | 58 (51.3) | 65 (57.5) | 44 (67.7) | 20 (30.8) |
| Unknown (5722) | 121 (2.1) | 103 (85.1) | 88 (72.7) | 43 (48.9) | 45 (51.1) |
| Pancreas (2920) | 81 (2.8) | 61 (75.3) | 56 (69.1) | 10 (17.9) | 45 (80.4) |
| Liver (2291) | 67 (2.9) | 43 (64.2) | 50 (74.6) | 19 (38.0) | 31 (62.0) |
| Small intestine (319) | 55 (17.2) | 43 (78.2) | 33 (60.0) | 12 (36.4) | 21 (63.6) |
| Thyroid (700) | 28 (4.0) | 11 (39.3) | 18 (64.3) | 5 (27.8) | 13 (72.2) |
| Testis (1018) | 26 (2.6) | 14 (53.8) | 21 (80.8) | 7 (33.3) | 14 (66.7) |
| Melanoma of skin (4070) | 18 (0.4) | 13 (72.2) | 14 (77.8) | 6 (42.9) | 8 (57.1) |
| Mesothelioma (1029) | 18 (1.7) | 12 (66.7) | 13 (72.2) | 5 (38.5) | 7 (53.8) |
| Other (3163) | 106 (3.4) | 53 (50.0) | 59 (55.7) | 18 (30.5) | 40 (67.8) |
| Multiple (3377) | 206 (6.1) | 74 (35.9) | 128 (62.1) | 11 (8.6) | 115 (89.8) |
| **Total (118 541)** | **6116 (5.2)** | **2629 (43.0)** | **3624 (59.3)** | **685 (18.9)** | **2899 (80.0)** |

Abbreviation: ICU, intensive care unit.

[a] Data are given as No. (%).

[b] Percentages do not sum to 100% because some ICU patients could not be matched to a hospital admission record.

Table 3. ICU and Hospital Mortality by Hospital Admission Type, Specialty, and Organ Support[a]

| Hospital Admission Specialty | Elective Admission: No Organ Support[b] | Elective Admission: Organ Support | Emergency Admission: No Organ Support[a] | Emergency Admission: Organ Support |
|---|---|---|---|---|
| **Patients Died in ICU** | | | | |
| Medical admission | | | | |
| % (95% CI) | 5.1 (1.4-12.5) | 21.1 (13.9-30.0) | 5.9 (3.0-10.4) | 41.7 (37.6-45.8) |
| No./Total No. | 4/79 | 23/109 | 11/185 | 240/576 |
| Surgical admission | | | | |
| % (95% CI) | 0.6 (0.3-1.2) | 14.5 (12.9-16.3) | 4.3 (3.0-6.0) | 24.5 (22.0-27.1) |
| No./Total No. | 9/1448 | 258/1775 | 32/744 | 275/1124 |
| **Patients Died in Hospital** | | | | |
| Medical admission | | | | |
| % (95% CI) | 12.7 (6.2-22.0) | 40.4 (31.1-50.2) | 32.4 (25.7-39.7) | 60.1 (55.9-64.1) |
| No./Total No. | 10/79 | 44/109 | 60/185 | 346/576 |
| Surgical admission | | | | |
| % (95% CI) | 4.1 (3.2-5.3) | 22.2 (20.3-24.2) | 14.7 (12.2-17.4) | 41.2 (38.3-44.1) |
| No./Total No. | 60/1448 | 394/1775 | 109/744 | 463/1124 |

Abbreviation: ICU, intensive care unit.

[a] Given as percentages of patients who died (95% CI) with numbers of patients.

[b] Includes patients with organ support not known.

(38.4% [95% CI, 34.7%-42.2%]) was twice that experienced by the 2899 patients admitted from a surgical specialty (18.4% [95% CI, 17.0%-19.8%]). The lowest ICU mortality of less than 1% (0.6% [95% CI, 0.3%-1.2%]) occurred among 1448 patients who were elective surgical admissions that did not receive organ support. In contrast, 41.7% (95% CI, 37.6%-45.8%) of 576 patients who were emergency medical admissions that had received organ support died in the ICU.

A total of 1486 patients (24.6% [95% CI, 23.5%-25.7%]) died during the hospital stay in which an ICU admission occurred; just under half of these deaths (10.5%) happened after discharge from ICU. The percentage of ICU patients who died in hospital was higher among those who received organ support (34.8% [95% CI, 33.2%-36.4%]) compared with those who had not (9.7% [95% CI, 8.6%-11.0%]). Following discharge from an ICU, hospital deaths among surgical patients who received

Table 4. Hospital Mortality by Cancer Site[a]

| Cancer Site (No. of Patients) | All Patients (n = 6040) | Emergency Admission (n = 2629) | Received Organ Support (n = 3584) | Emergency Admissions, Received Organ Support | | |
|---|---|---|---|---|---|---|
| | | | | Total (n = 1700) | Medical (n = 576) | Surgical (n = 1124) |
| Colorectal (2519) | 20.1 (18.5-21.7) | 27.8 (25.3-30.5) | 35.0 (32.3-37.8) | 40.7 (36.9-44.6) | 52.6 (43.1-61.9) | 38.2 (34.1-42.4) |
| Head and neck (634) | 11.8 (9.4-14.6) | 23.2 (16.9-30.4) | 12.1 (9.5-15.0) | 24.3 (17.4-32.2) | 36.1 (20.8-53.8) | 20.2 (13.0-29.2) |
| Stomach (454) | 23.3 (19.5-27.5) | 39.5 (31.0-48.5) | 38.6 (32.3-45.2) | 55.0 (43.5-66.2) | 66.7 (48.2-82.0) | 46.8 (32.1-61.9) |
| Lung (378) | 60.3 (55.2-65.3) | 67.8 (61.4-73.8) | 68.6 (62.8-73.9) | 71.7 (64.5-78.1) | 75.4 (67.1-82.5) | 62.0 (47.2-75.3) |
| Esophagus (386) | 20.2 (16.3-24.6) | 35.1 (24.4-47.1) | 25.8 (20.5-31.7) | 42.6 (29.2-56.8) | 72.2 (46.5-90.3) | 27.8 (14.2-45.2) |
| Kidney (245) | 14.3 (10.2-19.3) | 28.6 (17.9-41.3) | 23.9 (16.9-32.0) | 39.5 (25.0-55.6) | 28.6 (8.4-58.1) | 44.8 (26.4-64.3) |
| Bladder (181) | 27.1 (20.7-34.2) | 50.0 (37.6-62.4) | 32.5 (24.0-41.9) | 54.8 (38.7-70.2) | 53.8 (25.1-80.8) | 55.2 (35.7-73.6) |
| Breast (144) | 29.9 (22.5-38.0) | 42.6 (32.4-53.2) | 43.3 (32.9-54.2) | 53.7 (41.1-66.0) | 61.1 (43.5-76.9) | 45.2 (27.3-64.0) |
| Ovary (137) | 29.2 (21.7-37.6) | 33.3 (23.4-44.5) | 41.2 (29.4-53.8) | 46.5 (31.2-62.3) | 57.1 (34.0-78.2) | 36.4 (17.2-59.3) |
| Prostate (132) | 27.3 (19.9-35.7) | 43.7 (31.9-56.0) | 37.3 (27.0-48.7) | 50.0 (36.1-63.9) | 63.6 (40.7-82.8) | 40.6 (23.7-59.4) |
| Cervix and corpus uteri (112) | 18.8 (12.0-27.2) | 27.6 (16.7-40.9) | 29.7 (18.9-42.4) | 35.9 (21.2-52.8) | 35.0 (15.4-59.2) | 36.8 (16.3-61.6) |
| Unknown (120) | 72.5 (63.6-80.3) | 78.6 (69.5-86.1) | 76.1 (65.9-84.6) | 82.9 (72.5-90.6) | 82.5 (67.2-92.7) | 83.3 (67.2-93.6) |
| Pancreas (79) | 46.8 (35.5-58.4) | 47.5 (34.6-60.7) | 54.5 (40.6-68.0) | 56.8 (41.0-71.7) | 50.0 (18.7-81.3) | 58.8 (40.7-75.4) |
| Liver (67) | 56.7 (44.0-68.8) | 65.1 (49.1-79.0) | 58.0 (43.2-71.8) | 66.7 (47.2-82.7) | 56.3 (29.9-80.2) | 78.6 (49.2-95.3) |
| Small intestine (54) | 29.6 (18.0-43.6) | 27.9 (15.3-43.7) | 42.4 (25.5-60.8) | 38.5 (20.2-59.4) | 44.4 (13.7-78.8) | 35.3 (14.2-61.7) |
| Thyroid (28) | 10.7 (2.3-28.2) | 27.3 (6.0-61.0) | 5.6 (0.1-27.3) | 12.5 (0.3-52.7) | 0 (0-60.2) | 25.0 (0.6-80.6) |
| Testis (26) | 42.3 (23.4-63.1) | 71.4 (41.9-91.6) | 47.6 (25.7-70.2) | 75.0 (42.8-94.5) | 100 (59.0-100) | 40.0 (5.3-85.3) |
| Melanoma of skin (18) | 27.8 (9.7-53.5) | 30.8 (9.1-61.4) | 35.7 (12.8-64.9) | 36.4 (10.9-69.2) | 33.3 (4.3-77.7) | 40.0 (5.3-85.3) |
| Mesothelioma (17) | 47.1 (23.0-72.2) | 58.3 (27.7-84.8) | 58.3 (27.7-84.8) | 70.0 (34.8-93.3) | 80.0 (28.4-99.5) | 60.0 (14.7-94.7) |
| Other (105) | 26.7 (18.5-36.2) | 35.8 (23.1-50.2) | 39.7 (27.0-53.4) | 46.9 (29.1-65.3) | 36.4 (10.9-69.2) | 52.4 (29.8-74.3) |
| Multiple (204) | 17.6 (12.7-23.6) | 29.7 (19.7-41.5) | 26.2 (18.8-34.8) | 39.2 (25.8-53.9) | 55.5 (21.2-86.3) | 35.7 (21.6-52.0) |
| All (6040) | 24.6 (23.5-25.7) | 37.2 (35.3-39.1) | 34.8 (33.2-36.4) | 47.6 (45.2-50.0) | 60.1 (55.9-64.1) | 41.2 (38.3-44.1) |

[a] Data are given as percentages (95% CIs) of patients who died during the hospital stay in which they were admitted to an intensive care unit.

organ support increased by 11.2% to 29.6% (95% CI, 27.9%-31.3%) and among medical patients to 56.9% (95% CI, 53.1%-60.7%) (an 18.5% increase). Less than 5% of patients (4.1% [95% CI, 3.2%-5.3%]) who were elective surgical admissions that did not receive organ support died during their hospital stay (**Table 4**). In contrast, 60.1% (95% CI, 55.9%-64.1%) of patients who were emergency medical admissions and received organ support died in hospital.

The proportion of deaths during the hospital stay (Table 4) was highest for patients with cancers of unknown primary (72.5% [95% CI, 63.6%-80.3%]), lung cancer (60.3% [95% CI, 55.2%-65.3%]), and liver cancer (56.7% [95% CI, 44.0%-68.8%]). Hospital mortality was lowest for those with head and neck cancers (11.8% [95% CI, 9.4%-14.5%]), multiple cancers (17.6% [95% CI, 12.7%-23.6%]), kidney cancer (14.3% [95% CI, 10.2%-19.3%]), and thyroid cancer (10.7% [95% CI, 2.3%-28.2%]). For most cancers, ICU mortality was substantially higher among patients who were admitted as an emergency patient or had received organ support. Mortality was higher still among those patients admitted to medical specialties compared with those admitted to surgical specialties. For example, hospital mortality for medical and surgical patients with lung cancer who were emergency admissions and had received organ support was 75.4% (95% CI, 67.1%-82.5%) and 62.0% (95% CI, 47.2%-75.3%), respectively.

There was no clear trend in the proportions of patients with cancer admitted to ICU when examined by socioeconomic deprivation (eTable 2 in the Supplement). The proportion of patients who were emergency hospital admissions or who received organ support was higher in the most deprived quintile (46.6% [95% CI, 44.3%-48.9%] and 68.5% [95% CI, 66.3%-70.6%], respectively) compared with the least deprived quintile (41.1% [95% CI, 37.4%-44.9%], $P = .01$; and 58.2% [95% CI, 54.4%-61.9%], $P < .001$). Mortality among patients admitted from the most deprived areas was significantly higher (29.4% [95% CI, 27.3%-31.6%]) than that among those who lived in the least deprived areas (21.8% [95% CI, 18.7%-25.1%], $P < .001$).

There was significant variation in hospital mortality between units. This was not associated with the volume of patients admitted to ICU ($P = .76$) after adjusting for sex, age, organ support, admission type, admission specialty, SIMD, and calendar year (eTable 3 in the Supplement). There was a slight fall in overall hospital mortality over the study period (eFigure 3 in the Supplement), but this was not statistically significant ($P = .19$) (eTable 3 in the Supplement). The year-on-year odds ratio for hospital mortality was 0.98 (95% CI, 0.95-1.01). There was, however, significant variation in the temporal trend in mortality between ICU centers ($\sigma_{trend} = 0.04$ [95% CI, 0.02-0.09]).

## Discussion

In the first study of its kind, we have shown that just over 5% of patients with cancer developed a critical illness requiring ICU admission within 2 years of cancer diagnosis. The risk increased with age and was higher among men. There was a modest decline in the rate of ICU admission during the study period with higher emergency admissions, receipt of organ support, and hospital mortality among more socioeconomically deprived patients. Two-fifths of critical illness following a cancer diagnosis occurred among patients with colorectal cancers, but risks following breast cancer were among the lowest of all malignant neoplasms. Mortality was high, with 25% of all patients with cancer who developed a critical illness dying during the same hospital stay. We did not find a reduction in overall mortality during the study period. Critical illness may therefore play an important role in determining overall cancer outcomes and may help to explain variations in cancer survival.

Patients with cancer may develop critical illness for many reasons, but some broad patterns can be described. First, there is a group of patients for whom a stay in an ICU is offered as part of elective surgical treatment.[13] Such patients may have been assessed preoperatively as being at higher risk of complications from coexisting morbidities and therefore would benefit from the enhanced perioperative monitoring offered by an ICU/HDU environment. Their outcomes might be expected to be favorable because they have been selected for potentially curative treatment, and our results are consistent with this suggestion. Patients who are emergency admissions associated with a cancer diagnosis have poorer outcomes than those who are elective admissions, and patients who are medical admissions have poorer outcomes than those who are surgical admissions. Again, these observations partly reflect a group of surgical patients for whom the critical illness is likely to have been related to a perioperative insult rather than an ongoing inflammatory process that often occurs with medical patients. This is a consistent finding seen in ICU patients regardless of comorbidity and is often accounted for when using ICU mortality prediction scores.[12] While a direct comparison cannot be made because of differences in case mix, the observation that medical admissions had higher mortality than emergency and elective surgery admissions, respectively, has been made by Soares et al.[14] However, we are not aware of any published studies that explore the role of a critical illness as part of the overall determinants of survival in a nonselective cancer population.

We found that among emergency colorectal cancer admissions, hospital mortality was 38.2% in those admitted postoperatively compared with 52.6% for patients with a nonoperative diagnosis. Patients with cancer admitted to ICU with a medical diagnosis comprise a mixture of those who are experiencing the adverse effects of treatment, such as sepsis or tumor lysis syndrome,[15] and those experiencing progression of their cancer. Overall survival from breast cancer has been improving over several decades such that the 5-year relative survival rate is around 86% in Scotland.[16,17] We identified a subgroup of patients with breast cancer with much higher mortality, although we cannot say whether this was due to breast cancer itself or an incidental critical illness. There is increasing concern about use of systemic anticancer therapy within the last few weeks of patients' lives, and more detailed characterization of which patients are at greatest risk of critical illness requiring ICU care will provide further insights into outcomes.[18] Hospital mortality among those with nonsurgical lung cancer, at 75.4%, was considerably higher than that reported by Slatore et al[19] at 34% or by Soares et al[20] at 39%, and further analysis to compare case mix variables in these patients is needed to try to explain these differences.

A major strength of this study is that it is the first published research, to our knowledge, to describe risks of critical illness among patients with a comprehensive coverage of solid cancers. We believe that this population is representative of the overall population of patients with solid tumors who are admitted to an ICU with a critical illness in the United Kingdom. The large sample size, long observation period, and high quality of cancer registration and ICU data are also strengths.[21,22]

The principal limitation is that we could not identify patients whose critical illnesses did not result in admission to an ICU. We were further limited in our ability to differentiate HDU patients from ICU patients in combined units. Although we found significant variation in mortality between centers, we believe that this may reflect differences in case mix. While information on diagnoses is available through person-linked hospital discharge records, the level of clinical severity is not included. A prospective study is needed in which a range of physiological and functional measures is included to determine outcomes among patients with cancer whose critical illnesses do, and do not, result in ICU admission. Our study was carried out in one region of the United Kingdom, and, while we do not believe that admission policies are likely to be significantly different than those in other parts of the United Kingdom, further work to repeat our methodology in other geographic areas is needed.

## Conclusions

The United Kingdom has both poorer cancer outcomes and considerably lower provision of ICU beds than most other developed countries.[3,7] From our current results we cannot say whether greater provision of ICU beds would contribute to improvements in cancer survival in the United Kingdom. However, it might be hypothesized that if ICUs are effective in reducing mortality following a critical illness, increased surveillance for early signs of critical illness and greater capacity to offer ICU care to patients with cancer might be beneficial. Studies are needed in which outcomes of similar patients with cancer who are, and are not, admitted to ICU are compared.

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Invited Commentary

# Critical Care Utilization for Those With Cancer
## How Much Is Enough?

Knox H. Todd, MD, MPH, FACEP

**Intensive care units (ICUs)** provide specialized care that can be of high value to those with cancer who experience life-threatening complications of the disease or its treatment. The cost of providing intensive care is high, and unless the societal resources devoted to health care are limitless, we must continually decide how to best allocate resources to those who are likely to benefit.

While at one time, the diagnosis of cancer meant to clinicians that ICU admissions were largely futile, research suggests that, given appropriate patient selection, the benefits of critical care can be similar for those with and without a cancer diagnosis.[1] While intensive care can provide health benefits, particularly to those with reversible forms of organ failure, ICU care involves the possibility, and indeed the likelihood, of physical pain and emotional suffering. The provision of high-quality critical care requires consideration of both the likelihoods of such benefits and harms. Cross-national studies play a particularly important role in providing evidence for rational critical care practice. Counties differ widely in many forms of health care expenditures, including those related to ICU bed capacity. These capacity rates vary several-fold between the United States and Europe. A better understanding of this vari-